HbA1c LEVEL CORRELATION AS A PREDICTOR OF CORONARY ARTERY DISEASE AND ITS SEVERITY IN PATIENTS UNDERGOING CORONARY ANGIOGRAPHY

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ABSTRACT

BACKGROUND

To investigate relationship between glycated haemoglobin (HbA1c) level and coronary artery disease (CAD) severity.

METHODS

This cross sectional observational study was conducted over a period of six months, and 100 participants were enrolled and baseline characteristics were collected. Clinical presentations in terms of unstable angina, NSTEMI or acute myocardial infarction were diagnosed. Coronary angiography was performed on all participants to figure out the numbers of coronary artery stenosis in terms of non-significant stenosis (<50% stenosis), single or multiple vessels stenosis (≥50% stenosis). All participants were divided into subgroups according to two categories in terms of severity of clinical presentation (unstable angina, NSTEMI or acute myocardial infarction) and the number of coronary artery stenoses (single, and multiple vessels). Primary endpoint was to evaluate relationship between baseline HbA1c value and CAD severity.

RESULTS

Consistent to previous studies, participants with CAD had more risk factors such as age, smoking, low HDL-C. Notably, HbA1c level was more prominent in CAD group than that without CAD. As compared to unstable angina subgroup, HbA1c levels were gradually increased in NSTEMI and acute myocardial infarction groups. Similar trend was identified in another category in terms of higher HbA1c level corresponding to multivessel stenosis. Multivariate regression analyses showed that after adjusting for traditional risk factors as well as fasting blood glucose, HbA1c remained strongly associated with the severity of CAD.

CONCLUSION

HbA1c may be a useful indicator for CAD risk evaluation.

KEYWORDS

Glycated Haemoglobin, Coronary Artery Disease, Diabetes Mellitus.

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INTRODUCTION: Glycated haemoglobin or glycosylated haemoglobin (HbA1c) is a form of haemoglobin that is measured primarily to identify the average plasma glucose concentration over prolonged periods of time. It is a marker for average blood glucose levels over the previous three months prior to the measurement.

Evidence from epidemiological studies shown that as compared to fasting blood glucose, HbA1c was more strongly associated with the risks of atherosclerotic cardiovascular diseases (ASCVD) and mortality from any causes,[1, 2] which further supported the notion that HbA1c was superior to fasting blood glucose in predicting ASCVD outcomes. Truly, relationship between HbA1c and cardiovascular outcomes in populations without diabetes are still uncertain. Garg N and colleagues showed that in non-diabetics, HbA1c level has a linear incremental association with ASCVD.[3] Nonetheless, data from the Emerging Risk Factors Collaboration revealed that HbA1c merely added little incremental benefit for ASCVD risk prediction inpatients without known ASCVD and diabetes.[4]

One case-control study suggested that HbA1c is associated with coronary heart disease risk among apparently healthy, non-diabetic women and men and may be an important early clinical marker of disease risk.[5] HbA1c is significantly associated with the complexity of coronary lesions, an association that is even observed in non-diabetic adults.[6]

We aimed to develop a risk score incorporating HbA1c with traditional risk factors for the prediction of CAD. We

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hypothesised that a high HbA1c score would be associated with CAD based on the angiography.

METHODS:

Studied populations and protocols: Studied populations were enrolled from January 2016 to June 2016 after informed consent was obtained. This study was approved by the Ethical Committee of KIMS Hospital, Hubli. Cases were selected which satisfied inclusion and exclusion criteria.

Inclusion criteria - Patients presenting with acute coronary syndromes to cardiac intensive care unit.

Exclusion criteria - Patients with anaemia and chronic renal failure.

Coronary angiography was performed on all patients to know the number of coronary artery stenoses in terms of none-significant (< 50% stenosis), single or multiple vessel stenosis (≥50% stenosis). Baseline characteristics including age, gender, family history of ASCVD, smoking status, hypertension, serum levels of lipid profile, fasting blood glucose, and HbA1c were collected at admission. In order to better understand whether HbA1c level was associated with the severity of CAD, all participants were divided into different subgroups according to two major categories in terms of the severity of clinical presentation (unstable angina, NSTEMI or acute myocardial infarction) and the number of coronary artery stenoses (none, single, and multiple vessels stenosis).

Study endpoint: The primary endpoint of current study was to evaluate the relationship between HbA1c level and the severity of CAD. In addition, whether HbA1c was an independent risk indicator for the severity of CAD was also evaluated.

RESULTS:

Baseline characteristics: Totally 100 participants were enrolled and initially divided into two groups, namely without CAD group and CAD group, according to their coronary angiography examination. Since our current study was an observational study, it was understandable and rational that the risk factors or comorbidities were more prevalent in the CAD group than that of without CAD group.

Age (Yrs)	Frequency	Percent
21-30	2	2.0
31-40	12	12.0
41-50	22	22.0
51-60	38	38.0
61-70	22	22.0
71-80	4	4.0
Total	**100**	**100.0**
Table 1		

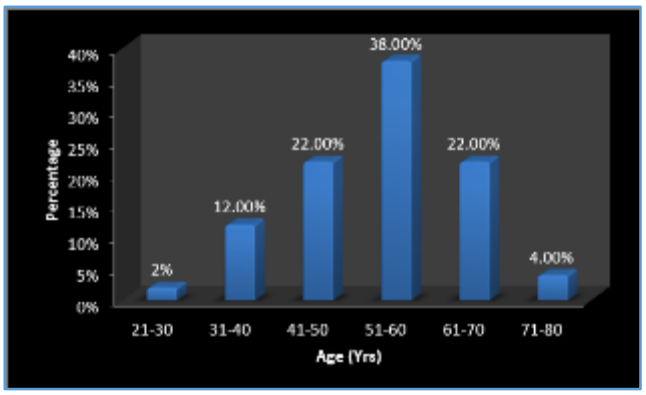

Fig. 1

In our study, most of the patients were in age group of fifty to sixty years.

Gender	Frequency	Percent
Male	72	72.0
Female	28	28.0
Total	**100**	**100.0**
Table 2		

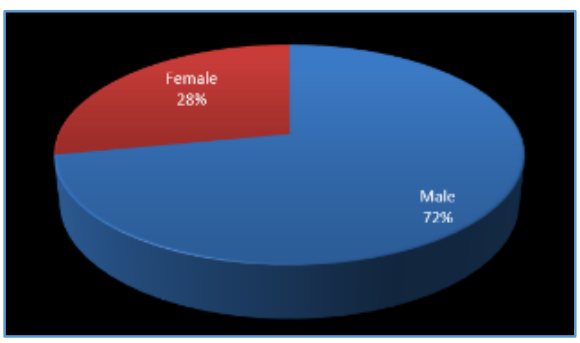

Fig. 2

The percentage of males were 72% compared to 28% females.

Hypertension	Frequency	Percent
Present	36	36.0
Absent	64	64.0
Total	**100**	**100.0**
Table 3		

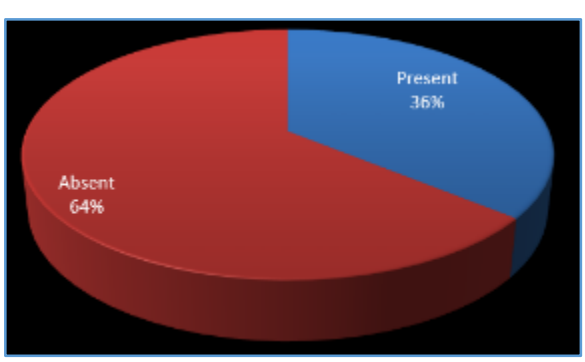

Fig. 3

Hypertension was present in 36% of the individuals.

Diabetes Mellitus	Frequency	Percent
Present	26	26.0
Absent	74	74.0
Total	**100**	**100.0**
Table 4		

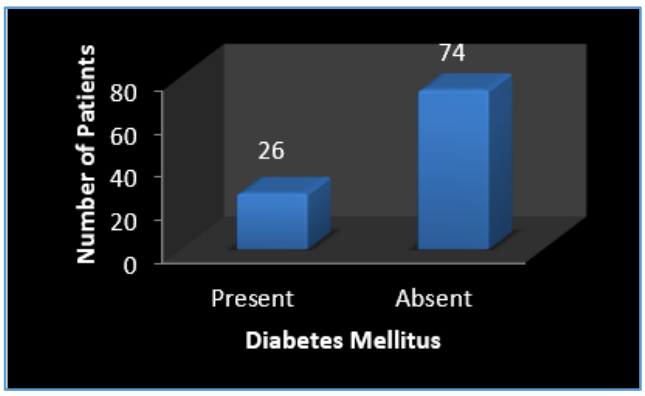

Fig. 4

26% of individuals were diabetic.

Ischaemic Heart Disease	Frequency	Percent
Present	12	12.0
Absent	88	88.0
Total	**100**	**100.0**
Table 5		

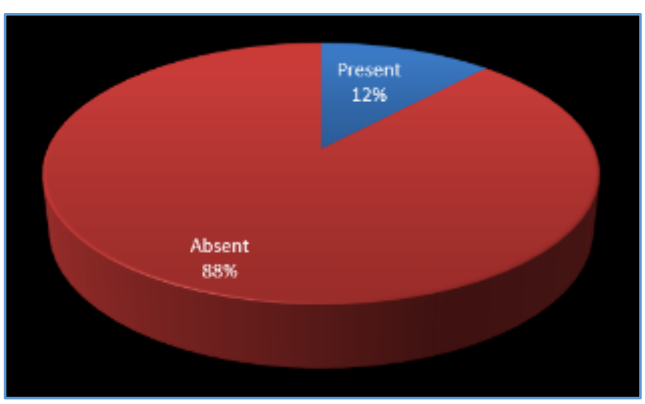

Fig. 5

Ischaemic heart disease was present in 12% of the individuals.

Family History	Frequency	Percent
Present	4	4.0
Absent	96	96.0
Total	**100**	**100.0**
Table 6		

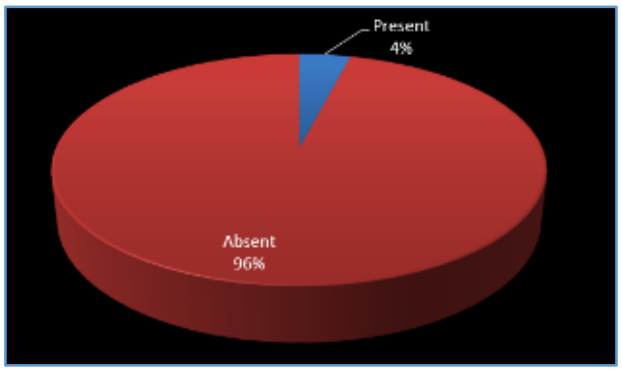

Fig. 6

4% of the individuals had positive family history of IHD.

Smoking	Frequency	Percent
Present	32	32.0
Absent	68	68.0
Total	**100**	**100.0**
Table 7		

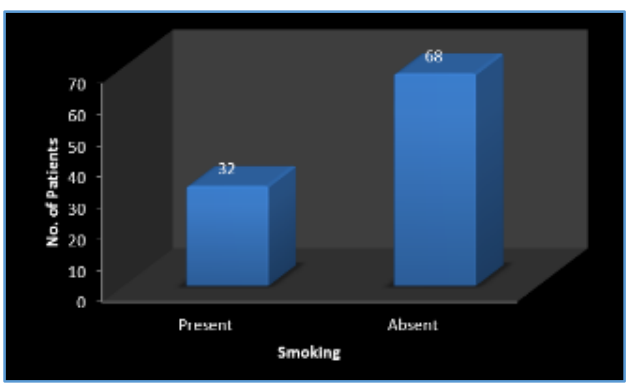

Fig. 7

4% of the individuals had positive family history of IHD.

HbA1c	Frequency	Percent
<6.5	20	20.0
6.5 to 8.5	48	48.0
8.5 to 10.5	26	26.0
>10.5	6	6.0
Total	**100**	**100.0**
Table 8		

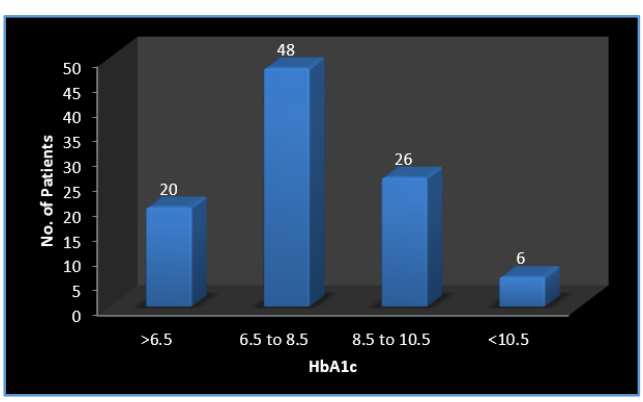

Fig. 8

HbA1C <6.5% in 20 cases, 6.5-8.5% in 48 cases, 8.5-10.5% in 26 individuals and >10 in 6 individuals.

CAD/NON-CAD	Frequency	Percent
CAD	80	80.0
NON-CAD	20	20.0
Total	**100**	**100.0**
Table 9		

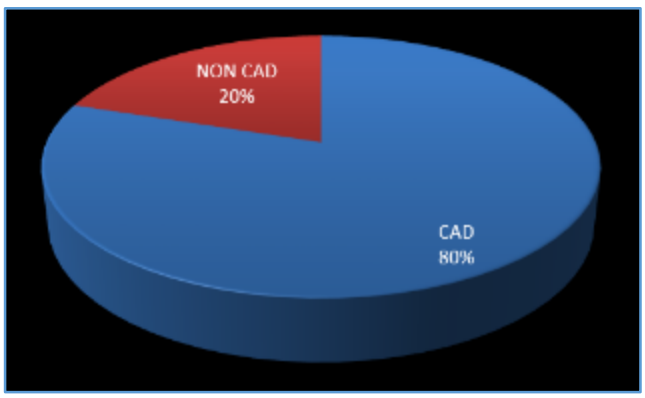

Fig. 9

80% of the individuals had significant CAD when compared to 20% who had no CAD (insignificant).

HbA1c	CAD	Non-CAD	Total	p value
<6.5	2	18	20	0.000
6.5 to 8.5	46	2	48	
8.5 to 10.5	26	0	26	
>10.5	6	0	6	
Total	**80**	**20**	**100**	
Table 10				

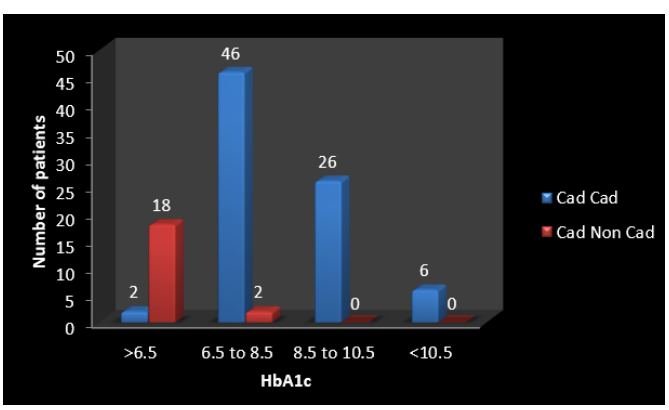

Fig. 10

Non-CAD patients had low HbA1c, CAD patients had high HbA1c levels.

HbA1c	SVD	DVD	TVD	Total
<6.5	0	0	0	0
6.5 to 8.5	42	2	2	46
8.5 to 10.5	0	18	6	24
>10.5	2	0	6	8
Total	**44**	**20**	**14**	**78**
Table 11				

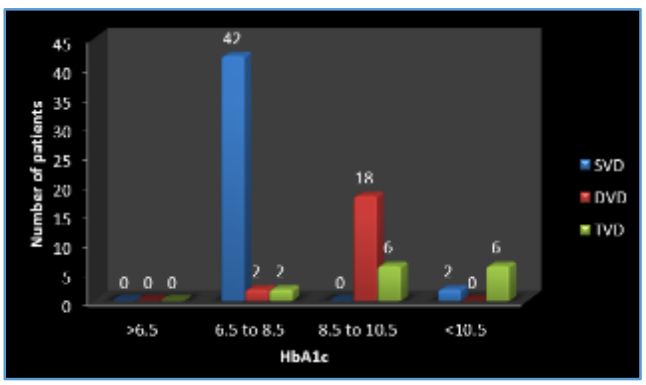

Fig. 11

Most of the patients with SVD had their HbA1c levels between 6.5-8.5%.

Most of the patients with DVD had their HbA1c levels between 8.5-10.5%.

Most of the patients with TVD had their HbA1c levels more than 10.5%.

Comparison of HbA1c levels among subgroups of CAD: In order to evaluate the relationship of HbA1c level and severity of CAD, all CAD patients were divided into different subgroups according to two major categories as described above. In the first category, all CAD patients were divided into unstable angina, NSTEMI and acute myocardial infarction groups. As shown in Figure 1, the difference of HbA1c level among each subgroup was significantly different, with a p value <0.05. In the second category, all CAD patients were divided into non-significant stenosis, single vessel stenosis and multiple vessels stenosis groups. As presented in Figure 2, the HbA1c level was significantly associated with the number of coronary artery stenoses, with a p value <0.001.

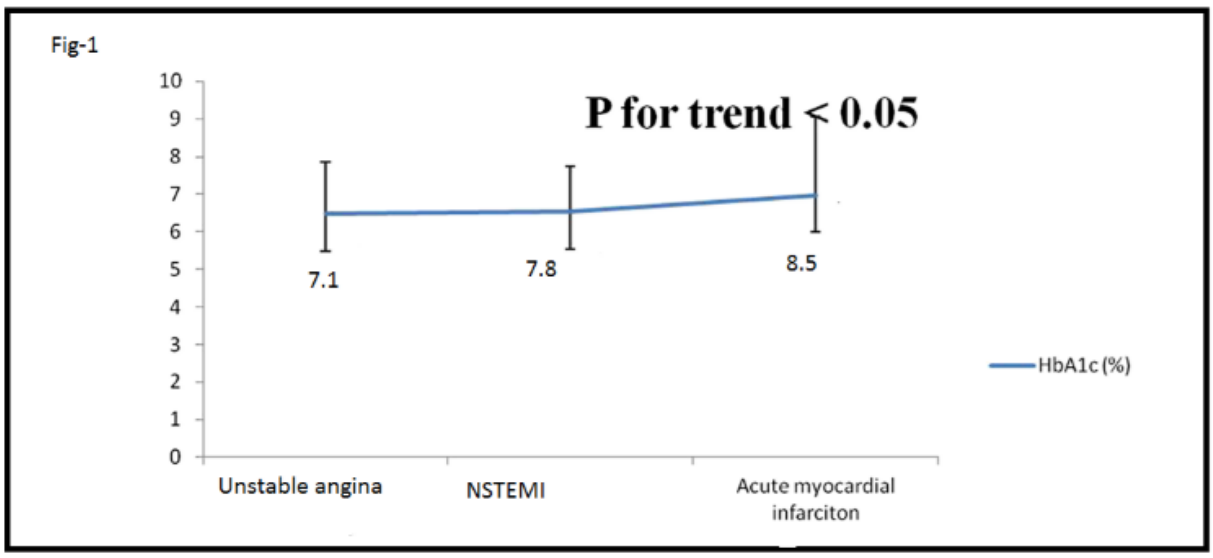

Fig. 12

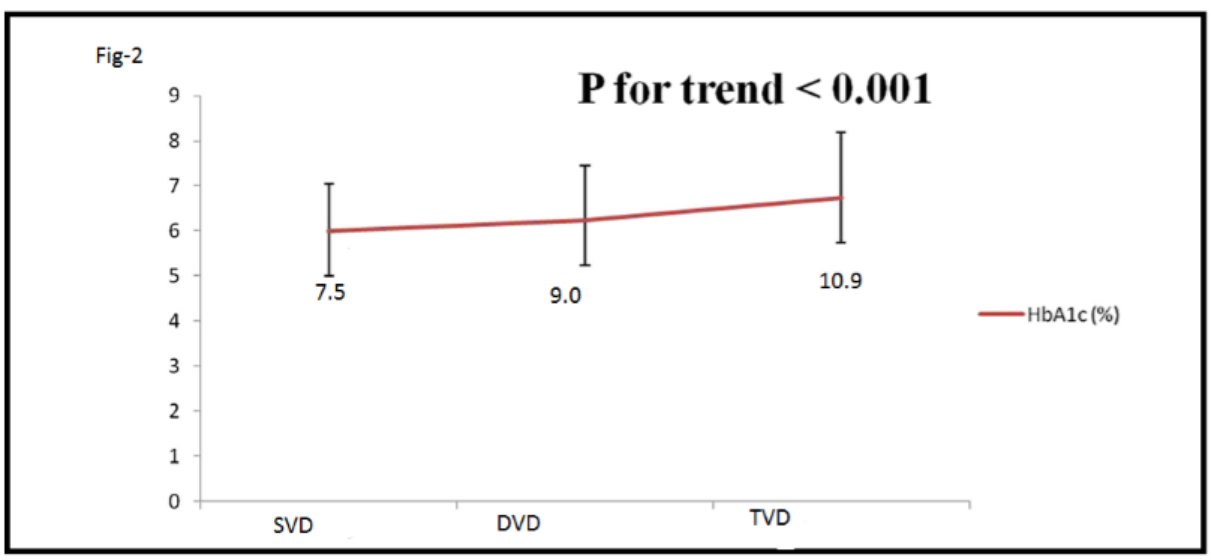

Fig. 13

DISCUSSION: Findings from our current study show that there is a significant association between HbA1c level and the severity of CAD, even after adjustment for traditional risk factors, and this relationship is independent of fasting blood glucose.

Knowingly, glycated haemoglobin is a stable parameter reflecting approximately 3 months of blood glucose levels and it has now been suggested using in clinical practice for long-term blood glucose assessment in diabetic patients.[7] HbA1c is calculated as the ratio of glycated to non-glycated N-terminal peptide of haemoglobin, and the HbA1c level has been universally recognised as an important indicator for microvascular complications in diabetic patients.[7, 8] Nevertheless, whether HbA1c level could also be used in macrovascular diseases (such as ASCVD) risk prediction is less clear.[9, 10]

Accordingly, CVD is the leading cause of morbidity and mortality worldwide and improvement of risk discrimination is imperative.[11] Previously, results from previous studies showed that for coronary heart diseases, risk discrimination was significantly enhanced when HbA1c was added in risk algorithm in non-diabetic patients.[12, 13]

Biologically, glycated haemoglobin is an advanced glycosylation end-product, and increased HbA1c level could reflect more generation of advanced glycosylation end-product, which might subsequently abundantly attach to vessel wall causing endothelial dysfunction and oxidative stress promotion.[14, 15] On the other hand, the binding of advanced glycosylation end-product might also result in inflammatory cytokines such as CRP over-production.[16] Increased CRP level has been found significantly associated with the instability of plaque.[17, 18]

Finally, increased advanced glycosylation end-product could interfere with endogenous fibrinolytic system which might result in higher risk of coronary artery stenosis.[19, 20] Future experimental and clinical studies are warranted to investigate whether reduced HbA1c level will improve atherosclerosis plaque stability. Other than the significant

association between HbA1c level and the severity of CAD, our current study also showed that increased HbA1c level was associated with multivessel stenosis.

As mentioned above, by means of increasing vascular permeability, promoting endothelium dysfunction, and enhancing inflammation and oxidative reaction, increased advanced glycosylation end-product might lead to multivessel stenosis.

Consistent with some previous epidemiological studies,[12, 13, 21] data from our study also revealed that after adjusting for traditional risk factors including age, smoking, HbA1c remained strongly associated with the severity of CAD. Notably, even after adjusting for fasting blood glucose, an independent risk factor for ASCVD and diabetes, there was still significant relationship between HbA1c and the severity of CAD, further supporting previous findings that HbA1c might be superior to fasting blood glucose in the respects of CVD risk discrimination. However, there was one distinctive discrepancy between our research and previous studies[12, 13, 21] that we concomitantly evaluated the relationship between HbA1c level and CAD severity including clinical scenario severity and the number of coronary artery stenoses. As compared to fasting blood glucose, HbA1c level reflecting both fasting and post-prandial blood glucose might also partially explain the superiority of HbA1c, because peak plasma glucose level might cause more severe damage to endothelium.[22, 23] Future study is warranted to investigate whether there is significant interaction between post-prandial blood glucose and HbA1c on CVD risk prediction.

CONCLUSION: Our observational study found out that HbA1c level was significantly associated with the severity of coronary artery diseases, further supporting the notion that HbA1c may be a useful and independent indicator for CVD risk evaluation.

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